DESCRIPTION

BLOOD TREATING FILTER EQUIPMENT AND

BLOOD TREATMENT METHOD

TECHNICAL FIELD

The present invention relates to a blood

5   treating filter equipment incorporating a filter

material to remove specific components efficiently from

a large amount of blood.

BACKGROUND ART

Recently, a requirement has been imposed for

10   a technology to remove a specific protein, leucocyte

and the like contained in blood for the purposes of a

blood extra-corporeal blood perfusion therapy for

autoimmune diseases or inflammatory bowel diseases such

as systemic lupus erythematosus, chronic or malignant

15   articular rheumatism, multiple sclerosis, ulcerative

colitis and Crohn's disease, or diseases such as

leukemia and cancer, or immuno-suppression before an

organ transplantation operation.

The blood treating filter equipment used for

20   these applications is required to have not only a high

removability but at the same time an ability to treat a

large amount (about 2 to 5 liters) of blood.

Until now, for example, a flat plate type

nonwoven fabric filter composed of extra fine fiber or

an equipment in which the filter is wound cylindrically
(JP-A-62-243561) have been proposed as a leucocyte
removal filter equipment. However, in a treatment of a
large amount of blood as described above with these

5 filters, a flow rate has to be reduced due to a
possible large pressure loss in the equipment depending
on a condition of the blood to be treated or when an
anticoagulant is added insufficiently or mixed
inadequately. This leads to a prolonged treatment

10 time. Thus, a further improvement in removal
efficiency has been required.

The inventors earnestly studied for a cause
of the above-mentioned rise of the pressure loss in a
filter. As a result, the following were revealed. In

15 a conventional filter, a large amount of an object to
be removed trapped in the filter narrows channels in
the filter resulting in making a smooth blood flow
difficult and raising a pressure. However, the rise of
the pressure loss in a filter described above was not

20 brought about as a resultor an object to be removed as
found in a conventional filter, but instead by
characterisnes specific to blood. In other words, the
inventors found out that the rise of the pressure loss
was caused by platelets and other coagulation factors

25 in blood which were activated by their sudden contact
with a filter material and formed a blocking membrane,
resulting in disturbing a smooth blood flow.

To avoid the problem described above, it is

considered to be effective to enlarge a surface area of the filter. However, a simple enlargement of a filter size extremely impairs operability and productivity of the equipment. Furthermore, an enlargement of a

5 surface area of a filter within a fixed volume of a filter material according to a conventional method lowers a removal efficiency for an object, due to a reduced filter thickness.

DISCLOSURE OF THE INVENTION

10 In view of the points described above, an object of the present invention is to provide a blood treating filter equipment with a high ability to avoid a pressure rise, which can inhibit local and abrupt activations of coagulation factors in blood, and remove

15 target substances to be removed from a large amount of blood with a high efficiency without reducing a treating rate.

In order to achieve the object described above, the present invention comprises the following

20 (1) and (2).

(1) A filter material, in which the following (a) and (b) are wound in an overlapped state, an end part of (b) is exposed to an outer circumferential surface or an inner circumferential surface of the filter

25 material, and both end faces of the filter material are sealed liquid-tightly,

wherein,

(a) is a blood treating filter layer, and

(b) is a sheet-like spacer layer through which blood flows more easily compared with said blood treating filter layer.

5   (2) A casing in which the filter material described above is installed, wherein the casing has a blood inlet and a blood outlet, the blood inlet leads to the side of an exposed end part of (b) on an outer circumferential surface or an inner circumferential

10   surface of the filter material described above, and the blood outlet leads to the opposite side to the blood inlet on an inner circumferential surface or an outer circumferential surface of the filter material described above.

15   BRIEF DESCRIPTION OF DRAWINGS

Fig. 1A is an example showing a state in which a spacer layer is substantially continuous.

Fig. 1B is an example showing a state in which a spacer layer is discontinuous.

20   Fig. 2 shows an example of actual spacer layers.

Fig. 3 shows an example of actual cylindrical shapes of a filter material.

Fig. 4 is a schematic drawing of a transverse

25   cross-section showing an example of the blood treating filter equipment of the present invention.

Fig. 5 is a schematic drawing of a transverse

cross-section showing an example of the blood treating filter equipment of the present invention.

Fig. 6 is a schematic drawing of a longitudinal cross-section showing an example of the

5 blood treating filter equipment of the present invention.

BEST MODE FOR CARRYING OUT THE INVENTION

The term "blood treating filter layer" in the present invention means a filter layer which can remove

10 a specified blood cell, protein or the like from a body fluid such as blood, and preferably a filter layer which can selectively capture a blood cell, protein or the like as an object to be removed.

As a form of the filter layer, those considered are such as a nonwoven fabric, a woven

15 considered are such as a nonwoven fabric, a woven cloth, a sheet of porous body or a sheet-like bag packed with particles. In the case when an object to be removed is leucocyte, a nonwoven fabric or a porous body gives preferable results from the view point of

20 removal efficiency.

The term "nonwoven fabric" means a fabric structure made of an assemblage of fibers composed of one or more layers without weaving and knitting. As a material for a fiber, a synthetic fiber, an inorganic

25 fiber or the like is used. Among them, a synthetic fiber, for example, fibers of polyethyleneterephthalate, polybutyleneterephthalate,

nylon, polypropylene, polyethylene, polystyrene, polyacrylonitrile and the like are preferably used.

A mean diameter of a fiber constituting the nonwoven fabric is not less than 0.3 μm and less than

5   5.0 μm, preferably not less than 0.4 μm and not more than 4.5 μm, more preferably not less than 0.5 μm and not more than 4.0 μm. A mean diameter less than 0.3 μm reduces a fluidity of blood resulting in a large pressure loss in an equipment, and that not less than

10 5.0 μm impairs a blood treating performance such as a leucocyte removal rate.

The mean diameter of a fiber constituting the nonwoven fabric of the present invention can be obtained, for example, by taking a photograph of fibers

15 constituting a nonwoven fabric using a scanning electron microscope, measuring diameters of 100 or more fibers chosen at random and calculating an arithmetical mean value of them.

And the term "porous body" in the present

20 invention means a structure having a continuous constitution like a three dimensional network with continuous open cells. Material for the porous body is not specially limited and includes a natural high polymer such as cellulose and its derivatives or a

25 polymer material such as polyolefin, polyamide, polyimide, polyurethane, polyester, polysulfone, polyacrylonitrile, polyethersulfone, poly(meth)acrylate, butadiene-acrylonitrile copolymer,

ethylene-vinylalcohol copolymer and polyvinylacetal, or
mixture thereof.

A mean pore size of the porous body is not
less than 1.0 μm and not more than 60 μm, preferably
5   not less than 2.0 μm and not more than 55 μm, more
preferably not less than 3.0 μm and not more than 50
μm. A mean diameter smaller than 1.0 μm reduces a
fluidity of blood resulting in a rise of a pressure
loss in an equipment, and that larger than 60 μm
10   impairs a blood treatment performance such as a
leucocyte removal rate.

The mean pore size in the present invention
is a value obtained by measuring by a pressure mercury
penetration method. The mean pore size is obtained
15   from a peak (mode) of a graph showing differential
volume of fine pores on an axis of ordinate and pore
size on an axis of abscissa by the pressure mercury
penetration method, for example, measuring with
Poresizer 9320 made by Shimazu Corp. For measurement
20   data by the pressure mercury penetration method, the
data measured at the pressure range of 1 - 2650 psia
are used.

In addition, in order to reduce a capture
rate for platelet and enable a selective adsorption and
25   capture for a target substance, a substrate surface of
a blood treating filter layer may be coated or grafted
with a polymer less capable of capturing platelets. A
ligand capable to selectively adsorb a specified

component such as blood cell or plasma protein may also
be coated or immobilized.

The term "thickness" of the blood treating
filter layer used in the present invention is defined
5   as the shortest distance when a line connecting a given
contacting face between a blood treating filter layer
and a spacer layer and another contacting face of an
adjacent layer crosses over the blood treating filter
layer only. This thickness is not less than 0.1 mm and
10 not more than 10.0 mm, preferably not less than 0.15 mm
and not more than 8.0 mm, more preferably not less than
0.2 mm and not more than 5.0 mm, though it depends on
the diameter of filter or the mean pore size. A
thickness of a filter layer more than 10.0 mm reduces a
15 length of the filter layer when the filter layer is
wound cylindrically within a limited volume of a filter
material, also reduces the length of the spacer layer
to be overlapped, and thus makes it difficult to avoid
a pressure rise. Also, a thickness less than 0.1 mm
20 extremely restricts a volume of the filter layer of the
portion to be overlapped with the spacer layer
resulting in a poor blood treating performance such as
a leucocyte removability.

The blood treating filter layer may be
25 composed of only one sheet-like filter layer or several
sheet-like filter layers of the same kind or multiple
kinds.

The term "spacer layer" in the present

invention is a layer through which blood flows more
easily compared with the blood treating filter layer,
and those used are such as a coarse net-like metal, a
synthetic resin, an inorganic fiber, a synthetic fiber,

5   or a nonwoven fabric made of a fiber having a diameter
larger than a nonwoven fabric used in the blood
treating filter layer and the like. The spacer layer
is overlapped and wound together with the blood
treating filter layer to create a space where blood

10 flows easier between the blood treating filter layers.
Preferably a width of the spacer layer is almost the
same as that of the blood treating filter layer,
provided that length means the whole length of the
spacer layer along a winding direction and width means

15 a length in a perpendicular direction to the winding
direction.

The spacer layer may be composed of only one
sheet or several sheet-like materials of the same kind
or multiple kinds similar to the blood treating filter

20 layer described above, but it is important that the
spacer layer is substantially continuous in the filter
material. Here, the term "substantially continuous"
means that any portion of the spacer layer is connected
continuously without an interruption by the blood

25 treating filter layer. Even if the spacer layer itself
is not continuous as shown in Fig. 1A, a gap structure
formed by winding a filter material can be
substantially continuous unless the gap structure is

intercepted by the blood treating filter layer. The spacer layer can become discontinuous as shown in Fig. 1B, but in the present invention, only a substantially continuous part from a blood inlet side is called a

5 spacer layer, and a part in a downstream from the portion intercepted by a blood treating filter layer is not called a spacer layer.

The term "volume ratio of spacer section" in the present invention means a ratio of a volume

10 occupied by a spacer section to a volume occupied by a filter section. If a thickness of the spacer section is uniform and a filter material is cylindrical, then the volume ratio of spacer section is expressed by the formula (1) described hereinbelow. The term "spacer

15 section" means a portion of the spacer layer sandwiched by the blood treating filter layers in its inner and outer sides and leading to the blood inlet side, except a part exposed on the outermost or innermost circumferential surfaces of the filter material or a

20 part disconnected from the blood inlet side in the filter material. The volume of the spacer section is calculated as a volume of the spacer section supposing that it is sheet-like. The term "filter section" in the present invention means a part of the filter

25 corresponding to a part of the spacer material except the part of the spacer layer exposed on the outermost or innermost circumferential surfaces.

Volume ratio of spacer section = Volume of spacer

section [L x n x d] / Volume of filter section [V]

(1)

wherein,

Volume of filter section [V] = L x π x (R^2 - r^2)

5   R and r are calculated based on the lengths

of the circumferences of the outermost and innermost

layers of a blood treating filter layer, respectively,

supposing that a cross-section of the filter material

is round having a radius.

10   R: Radius of the outermost circumferential

layer of the filter section (mm)

          r: Radius of the innermost circumferential

layer of the filter section (mm)

          L: Width of the filter section (= Width of

15   the spacer section) (mm)

          V: Volume of the filter section (mm^3)

          d: Thickness of the spacer section (mm)

          n: Length of the spacer section (mm)

          The value of the volume ratio of spacer

20   section is not less than 0.3 and not more than 0.7,

preferably not less than 0.35 and not more than 0.65,

and more preferably not less than 0.4 and not more than

0.6. The value of the volume ratio of spacer section

less than 0.3 reduces an ability to avoid a pressure

25   rise. The value over 0.7 decreases a volume of a blood

treating filter layer, and impairs a blood treatment

performance such as leucocyte removability because it

decreases a frequency of a contact of blood with a

blood treating filter layer due to an overwhelmingly
increased blood flow to a spacer layer.

The term "spacer thickness" as used in the
present invention means the shortest distance when a
5   line connecting a given contacting face between a blood
treating filter layer and a spacer layer and another
contacting face of an adjacent layer crosses over the
spacer layer only, and is not less than 0.5 mm and not
more than 2.0 mm, preferably not less than 0.6 mm and
10 not more than 1.9 mm, and more preferably not less than
0.7 mm and not more than 1.8 mm. The value of the
spacer thickness less than 0.5 mm reduces an ability to
avoid a pressure rise. The value over 2.0 mm decreases
a volume of a blood treating filter layer, and impairs
15 a blood treating performance such as leucocyte
removability because it decreases a frequency of a
contact of blood with a blood treating filter layer due
to an overwhelmingly increased blood flow to a spacer
layer.

20   Furthermore, the spacer section may have
forms such as illustrated in Fig. 2, and is overlapped
with a blood treating filter layer. In Fig. 2, blank
rectangles in the background express blood treating
filters, and assemblages of small squares drawn on them
25 express spacer layers, respectively. Preferably, a
width of the spacer section is almost the same as that
of the blood treating filter layer provided that length
means the whole length along a winding direction of the

layer and width means a length along a perpendicular direction to the winding direction. A length of the spacer section is not necessarily almost the same as that of the blood treating filter layer, but a length

5   from an end at a blood inlet side where at least overlapping with a blood treating filter layer starts may be about 1/2 or more, preferably 2/3 or more, and more preferably 3/4 or more of the whole length of a blood treating filter layer. If the length of an

10 overlapped spacer layer to a blood treating filter layer is shorter than this, a desired avoidance for a pressure rise can not be attained in a blood treatment.

In order to recover blood from the equipment after a blood treatment is finished, blood is sometimes

15 pushed out by air pressure by introducing air into the equipment instead of flowing an aqueous solution such as saline. In consideration of such an operation, a structure in which the entire circumferential surface on the blood outlet side of a filter section is covered

20 with a filter layer is desirable for easier recovery of blood remaining in the equipment, because a blood treatment can be finished within a short period. On the other hand, a structure in which a spacer layer is exposed at both of an outer and an inner ends of the

25 filter section is most desirable to achieve more superior ability for avoiding a pressure rise besides keeping a high blood treatment performance such as a leucocyte removability. That is, this structure has a

high blood treatment performance such as a leucocyte

removability although an outer and an inner

circumferential layers of the filter section are

communicating with each other through a spacer layer.

5   The spacer layer exhibits the effects

mentioned above by exposing its end at a blood inlet

side of a blood treating filter layer. When a blood

inlet side is on the outer circumferential surface

side, a material constituting a spacer layer may be

10   extended from a space between blood treating filter

layers and exposed on an outer circumferential surface

of a filter material, and used as a support

continuously covering a whole area of the outer

circumferential surface of the filter material (Refer

15   to (9) in Fig. 4). Since a uniform space corresponding

to a thickness of the support is created between an

inside wall of a case and a blood treating filter layer

by the presence of the support on a whole area of an

outer circumference surface like a spacer layer,

20   introduced blood to be treated can easily spread to the

whole area of the outer circumferential surface of the

filter material. Preferably such a support is

continuous to a spacer layer from the view point of

easy manufacturing, but may be wound on the outer

25   circumferential surface of the filter material

independently from the spacer layer. As such a

support, a mesh and the like having many apertures to

make blood flow easier than through a blood treating

filter layer can be used.

The present invention is new described mainly for a case in which a blood inlet side is on the outer circumferential surface side of a filter material as an

5 example. A filter material composed of a blood treating filter layer and a spacer layer is, for example, wound in a hollow cylindrical shape having a cylindrical space in a central part. The hollow part inside of the filter material becomes a channel for

10 blood recovery after components to be removed such as leucocytes are eliminated from blood. Any shape of the hollow cylinder may be accepted as illustrated in Fig.3, but a cylindrical shape is the most preferable from the view point of a fluidity of blood through the

15 spacer layer and productivity of the filter material. Size of the filter material cannot be determined unconditionally because it depends on an amount of blood to be treated and a structure of the filter material to be adopted, but roughly an outer diameter

20 of 30 - 50 mm and a height of 100 - 250 mm is preferable for treating approximately 3 liters of blood.

A ratio of an outer diameter to a length between both end faces of the cylindrical filter

25 material is desirably around 1 : 10 - 1 : 2. Within a fixed volume of a filter material, the length between both end faces shorter than 1 : 2 reduces an ability to avoid a pressure rise because a flow of blood to a

16

spacer layer is restricted due to a narrowed entrance

into a spacer layer. The length between both end faces

longer than 1 : 10 lowers a performance because of a

reduced thickness of a blood treating filter layer, and

5 makes it difficult to wind a blood treating filter

layer together with a spacer layer.

In a hollow space in the center of a filter

material, preferably a support contacts an inner

circumferential surface [(10) in Figs. 4 and 5] and

10 consists of a pipe and the like having a mesh or a

porous part in order to support an inner

circumferential surface of a filter material and creame

a hollow space. The size of the hollow section of a

filter material should be properly determined depending

15 on a size of the filter material, that is, an outer

diameter, a thickness and the like of the filter

material.

In the present invention, the filter material

is installed in a cylindrical case having a similar

20 size, and both end faces are liquid-tightly sealed so

that blood cannot pass through. For sealing, a

material which has a superior compatibility in contact

with blood and is suitable for liquid-tight sealing may

be used. More specifically, a known synthetic resin

25 such as a urethane and a silicone can be used.

A blood inlet may be located in any desired

position of the case so long as blood to be treated can

be fed therefrom to the outer circumferential surface

side of the filter material having both ends sealed.
Preferably it should be located in an uppermost part of
a cylindrical case so that blood to be treated can
evenly flow into the outer circumferential surface of
5 the filter material and be dispersed radially for the
filter material to be efficiently utilized.

An embodiment of the blood treating filter
equipment of the present invention is now explained
more specifically using Figs. 4 - 6.

10 The blood treating filter equipment 1 is
composed of the filter material 4 wound in a hollow
cylindrical shape and the case 2 having the blood inlet
3 and the blood outlet 6. The filter material is
liquid-tightly sealed at both end faces with the
15 adhesive 5, and installed in the case 2 so that its
outer side and inner side communicate with the blood
inlet 3 and the blood outlet 6, respectively.

The blood to be treated flows into the blood
treating filter equipment 1 from the blood inlet 3.
20 Both end faces of the hollow cylindrical filter
material 4 are liquid-tightly sealed and the blood
cannot pass through. Therefore, through the outermost
layer of the blood treating filter layer 7, the
outermost layer of the spacer layer 8 or an outer end
25 of the spacer layer 8 which is constituting an outer
circumferential surface of the filter material, the
blood gradually permeates into the inside of the filter
material with components to be removed being captured,

gathers in a hollow part at the center of the filter

material after passing through the cylindrical filter

material, and exits from the equipment through the

blood outlet 6 communicating with the hollow part.

5   The flow of blood in the filter material is a

combined stream of two components: a flow that

penetrates into the blood treating filter layer 7

accompanied with the capture or removal of components

to be removed such as leucocyte, and another flow that

10   runs along the spacer layer 8. As a result, the blood

spreads to both the outer and inner circumferential

parts of the filter material soon after starting a

treatment, and a sharply reduced flow resistance

enables a continuation of a smooth and efficient

15   removal of the objects throughout the whole period of

time from the start to the end of the treatment.

By the actions described above, a blood flow

spirally penetrating toward an inner circumferential

surface of the cylindrical filter along with the spacer

20   layer in addition to a blood flow crossing over the

blood treating filter layers in an outer part of the

filter material can enlarge a contact area between

blood and the blood treating filter layer in the

initial stage of the start of the treatment. It is

25   believed that this enables inhibiting a local and

abrupt activation of blood coagulation components

caused by a gathering of the blood into a narrow

surface area of the filter. Furthermore, even when a

blood treating filter layer located in an outer

circumferential surface side of the filter material is

blocked, since another blood flow channel to an inner

circumferential surface side of the filter material has

5   been created, a pressure loss does not rise and a

treating rate can be kept constant until the end of a

treating period.

The present invention will now be explained

more concretely by Examples.

10   Examples 1 - 4 and 6 - 8, and Comparative Examples 1 -

2

As a blood treating filter layer for the

purpose of leucocyte removal (hereinafter referred to

as leucocyte removal filter layer), a nonwoven fabric

15   (coarseness 66 g/m^2, thickness 0.4 mm) made of a

polyester (PET: density 1.38 g/cm^3) fiber having a mean

diameter of 1.7 μm was used in a two-ply, which had a

width of 150 mm and a length of b (mm) shown in Table

1. A mesh (mesh size 8 mm, thickness d mm) made of

20   polyethylene with a width of 150 mm was also used as a

spacer layer. Both layers were wound around a

cylindrical mesh (mesh size 8 mm, thickness 1.0 mm,

outer diameter 2r mm) made of polyethylene being

overlapped each other, so that, when they were wound

25   like a roll, the spacer layer was overlapped with an

outer filter layer by a spacer section length of n (mm)

from an outer end of the filter layer and a part of the

spacer layer was exposed on the most outer filter

layer, to give a hollow cylindrical filter material

with an outer diameter of 36 mm as shown in Fig. 5.

Both end faces along the cylindrical axis of

5 this filter material were sealed with a urethane.

Then, the filter material was installed in a

cylindrical polycarbonate case with an inner diameter

of 41 mm and a length of 150 mm, which had a blood

inlet and a blood outlet in the top part and the bottom

10 part of the case, respectively, so that an outer and an

inner circumferential surfaces of the filter material

communicated with the blood inlet and the blood outlet

of the case, respectively, to give a leucocyte removal

filter equipment.

15 Example 5

As a leucocyte removal filter layer, a porous

material (mean pore size 30 μm, thickness 1.0 mm) made

of a polyvinylformal with a width of 150 mm and a

length of 680 mm was used. Also a mesh made of

20 polyethylene (mesh size 8 mm, thickness 1.0 mm) with a

width of 150 mm and a length of spacer section of 550

mm was used as a spacer layer. These two layers were

wound as in Example 1 - 4, to give a hollow filter

material with an outer diameter of 36 mm as shown in

25 Fig. 5.

Both end faces along the cylindrical axis of

this filter material were sealed with a urethane.

Then, the filter material was installed in a

cylindrical polycarbonate case with an inner diameter

of 41 mm and a length of 150 mm, which had a blood

inlet and a blood outlet in the top part and the bottom

5   part of the case, respectively, so that an outer and an

inner circumferential surfaces of the filter material

communicated with the blood inlet and the blood outlet

of the case, respectively, to give a leucocyte removal

filter equipment.

10   Comparative Example 1

As a leucocyte removal filter layer, a

nonwoven fabric (coarseness 66 g/m^2, thickness 0.4 mm)

made of a polyester (PET: density 1.38 g/cm^3) fiber

having a mean diameter of 1.7 μm was used in a two-ply,

15   which had a width of 150 mm and a length of 680 mm.

This layer was wound around a cylindrical mesh made of

polyethylene (mesh size 8 mm, thickness 1.0 mm, outer

diameter 22 mm), to give a hollow cylindrical filter

material with an outer diameter of 36 mm.

20   Both end faces along the cylindrical axis of

this filter material were sealed with a urethane.

Then, the filter material was installed in a

cylindrical polycarbonate case with an inner diameter

of 41 mm and a length of 150 mm, which had a blood

25   inlet and a blood outlet in the top part and the bottom

part of the case, respectively, so that an outer and an

inner circumferential surfaces of the filter material

communicated with the blood inlet and the blood outlet
of the case, respectively, to give a leucocyte removal
filter equipment.

Comparative Example 2

5   As a leucocyte removal filter layer, a
nonwoven fabric (coarseness 66 g/m^2, thickness 0.4 mm)
made of a polyester (PET: density 1.38 g/cm^3) fiber
having a mean diameter of 1.7 μm was used in a two-ply,
which had a width of 150 mm and a length of 680 mm. A
10 mesh (mesh size 8 mm, thickness 2 mm) made of
polyethylene was also used as a spacer layer with a
width of 150 mm and a length of 380 mm. Both layers
were wound around a cylindrical mesh (mesh size 8 mm,
thickness 1.0 mm, outer diameter 8.0 mm) being
15 overlapped each other, so that, when they were wound
like a roll, the spacer layer was overlapped with an
outer filter layer by the spacer section length of 380
mm from an outer end of the filter layer and the spacer
layer was not exposed at the outer end, to give a
20 hollow cylindrical filter material with an outer
diameter of 36 mm.
          Both end faces along the cylindrical axis of
this filter material were sealed with a urethane.
Then, the filter material was installed in a
25 cylindrical polycarbonate case with an inner diameter
of 41 mm and a length of 150 mm, which had a blood
inlet and a blood outlet in the top part and the bottom

part of the case, respectively, so that an outer and an

inner circumferential surfaces of the filter material

communicated with the blood inlet and the blood outlet

of the case, respectively, to give a leucocyte removal

5   filter equipment.

Experimental Example 1

Three liters of fresh bovine blood (leucocyte

count 4,800 - 6,800 cells/μl, platelet count 163,000 -

239,000 platelets/μl) added with heparin (4,000 U/l) as

10   an anticoagulant was passed through each of the filters

of the Examples and Comparative Examples described

above at 37℃ and at the flow rate of 50 ml/min using a

blood pump, then leucocyte removal rates and pressure

losses of the equipments before and after the

15   filtration were studied.

Blood samples were collected at each of

inlets and outlets of the filter equipments followed by

counting their leucocyte counts [cell/μl] using the

Turk's staining method. Leucocyte removal rates were

20   calculated from the values of the leucocyte counts as

follows:

Leucocyte removal rate [%] = (Leucocyte count of the

blood at the inlet side - Leucocyte count of the blood

at the outlet side) x 100 / leucocyte count of the

25   blood at the inlet side

Pressure losses were obtained by connecting

pressure gauges in both the inlet and outlet sides of

the blood circuit of the equipment and calculating as

follows:

Pressure loss [mmHg] = Pressure at the inlet side -

Pressure at the outlet side

5   Leucocyte removal treatments were tried by

passing 3 liters of the blood to be treated each at the

flow rate of 50 ml/min. An index for a resistance for

filter blocking due to activated blood coagulation

components was evaluated as a rate of the number of

10 runs in which the blood treatments were achieved with

pressure losses of the equipment under 150 mmHg. Each

experiment was carried out with 15 runs.

        Specifications of the filters used in the

Examples and the Comparative Examples and their results

15 are shown in Table 1 and Table 2 respectively. In

these Tables, the term "Length of Spacer Section" means

a length of overlapped part of the mesh between the

leucocyte removal filter layers and is expressed by a

length of the filter layer in contact with the mesh,

20 excluding an exposed part on the outermost and/or

innermost circumferential surface of the filter

material. And the term "Flow Achieving Rate" shows an

achieving rate of the blood treatments in which 3

liters of blood could be treated without experiencing a

25 pressure loss of 150 mmHg or higher. Furthermore, the

specification of each filter material was evaluated by

calculating a total performance index which was a value

obtained by dividing a product of the Leucocyte Removal

Rate and the Flow Achieving Rate by 100.

Example 9

As a leucocyte removal filter layer, a
nonwoven fabric (coarseness 66 g/m^2, thickness 0.4 mm)
5   made of a polyester (PET: density 1.38 g/cm^3) fiber
having a mean diameter of 1.7 μm was used in a two-ply,
which had a width and a length of 40 mm and 60 mm,
respectively. A mesh (mesh size 8 mm) made of
polyethylene was also used as a spacer layer with a
10   width of 40 mm. Both layers were wound like a roll so
that, when they were wound like a roll, the spacer
layer was overlapped with the outer filter layer by a
spacer section length of 60 mm from the outer end of
the filter layer and a part of the spacer layer was
15   exposed on the outermost filter layer, to give a hollow
cylindrical filter material with an outer diameter of
11 mm and an inner diameter of 6 mm as shown in Fig. 4.

Both end faces along the cylindrical axis of
this filter material were sealed with a urethane.
20   Then, the filter material was installed in a
cylindrical polypropylene case with an inner diameter
of 13 mm and a length of 45 mm, which had a blood inlet
and a blood outlet in the top part and the bottom part
of the case, respectively, so that an outer and an
25   inner circumferential surfaces of the filter material
communicated with the blood inlet and the blood outlet
of the case, respectively, to give a leucocyte removal

filter equipment.

Comparative Example 3

As a leucocyte removal filter layer, a nonwoven fabric (coarseness 66 g/m^2, thickness 0.4 mm)

5 made of a polyester (PET: density 1.38 g/cm^3) fiber having a mean diameter of 1.7 μm was used in a two-ply, which had a width of 40 mm and a length of 60 mm. This layer was wound like a roll to give a hollow cylindrical filter material with an outer diameter of

10 11 mm and an inner diameter of 8 mm.

Both end faces along the cylindrical axis of this filter material were sealed with a urethane. Then, the filter material was installed in a cylindrical polypropylene case with an inner diameter

15 of 13 mm and a length of 45 mm, which had a blood inlet and a blood outlet in the top part and the bottom part of the case, respectively, so that an outer and an inner circumferential surfaces of the filter material communicated with the blood inlet and the blood outlet

20 of the case, respectively, to give a leucocyte removal filter equipment.

Experimental Example 2

Fifteen milliliters of human fresh blood (leucocyte count 4,650 cells/μl, platelet count 204,000

25 platelets/μl) added with ACD-A as an anticoagulant was passed through each of the filter equipments of the

Example 9 and the Comparative Example 4 at the flow

rate of 1 ml/min using a blood pump, then leucocyte

removal rates before and after the filtration and also

concentrations of PF4 (platelet 4th factor) and β-TG

5 (β-thromboglobulin) as indices for activities of the

platelet before and after the filtration were measured.

Blood samples were collected at each of the

inlets and the outlets of the filter equipments

followed by counting their leucocyte counts [cell/μl]

10 using the Turk's staining method. Leucocyte removal

rates were calculated from the values of the leucocyte

counts as follows:

Leucocyte removal rate [%] = (Leucocyte count of the

blood at the inlet side - Leucocyte count of the blood

15 at the outlet side) x 100 / leucocyte count of the

blood at the inlet side

Results are shown in Table 3.

It is found that the activation of platelet

is inhibited in the cases of the filter material

20 structures of the present invention compared with the

conventional filter structures.

Table 1

	2R Outer Diameter of Filter Section (mm)	2r Inner Diameter of Filter Section (mm)	L Width of Filter or Spacer Section (mm)	V Volume of Filter Section (mm³)	b Length of Leucocyte Removal Layer (mm)	d Thickness of Spacer Section (mm)	n Length of Spacer Section (mm)	D Volume Ratio of Spacer Section
Example 1	36	8	150	145000	680	1.0	550	0.57
Example 2	36	8	150	145000	680	1.0	340	0.45
Example 3	36	16	150	123000	680	0.5	650	0.40
Example 4	36	8	150	145000	380	2.0	340	0.70
Example 5	36	8	150	145000	680	1.0	550	0.57
Example 6	36	18	150	115000	680	0.3	650	0.26
Example 7	36	8	150	145000	680	1.0	120	0.12
Example 8	36	8	150	145000	320	2.5	300	0.78
Comparative Example 1	36	22	150	96000	680	0.0	0	0.00
Comparative Example 2	36	8	150	145000	380	2.0	340	0.70

Table 2

	A Leucocyte Removability (%)	B Flow Achieving Rate (%)	C Total Performance Index (AxB) / 100
Example 1	97.6	100	97.6
Example 2	98.5	80	78.8
Example 3	98.1	87	85.3
Example 4	91.5	100	91.5
Example 5	96.5	100	96.5
Example 6	97.0	53	51.4
Example 7	98.5	60	59.1
Example 8	58.6	100	58.6
Comparative Example 1	98.9	33	32.6
Comparative Example 2	92.2	40	36.9

Table 3

	Leucocyte Removability (%)	PF4 (ng/ml)	β-TG (ng/ml)
Example 9	97.6	102	976
Comparative Example 4	100	208	1620

Industrial applicability

Since the blood treating filter equipment of
the present invention does not show a blocking of the
filter material due to activated coagulation components
5   in the blood even when a large amount of blood on the
order of several liters is treated, removal of target
substances from a total amount of a desired volume of
blood can be performed at high efficiency.